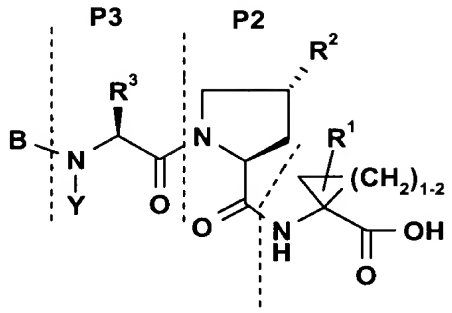


(I)

wherein **B** is H, a C_6 or C_{10} aryl, C_{7-16} aralkyl; Het or (lower alkyl)-Het, all of which optionally substituted with C_{1-6} alkyl; C_{1-6} alkoxy; C_{1-6} alkanoyl; hydroxy; hydroxyalkyl; halo; haloalkyl; nitro; cyano; cyanoalkyl; amino optionally substituted with C_{1-6} alkyl; amido; or (lower alkyl)amide; or **B** is an acyl derivative of formula $\mathbf{R_4}$-C(O)-; a carboxyl derivative of formula $\mathbf{R_4}$-O-C(O)-; an amide derivative of formula $\mathbf{R_4}$-N($\mathbf{R_5}$)-C(O)-; a thioamide derivative of formula $\mathbf{R_4}$-N($\mathbf{R_5}$)-C(S)-;or a sulfonyl derivative of formula $\mathbf{R_4}$-SO_2 wherein

$\mathbf{R_4}$ is (i) C_{1-10} alkyl optionally substituted with carboxyl, C_{1-6} alkanoyl, hydroxy, C_{1-6} alkoxy, amino optionally mono- or di-substituted with C_{1-6} alkyl, amido, or (lower alkyl) amide;
(ii) C_{3-7} cycloalkyl, C_{3-7} cycloalkoxy, or C_{4-10} alkylcycloalkyl, all optionally substituted with hydroxy, carboxyl, (C_{1-6} alkoxy)carbonyl, amino optionally mono- or di-substituted with C_{1-6} alkyl, amido, or (lower alkyl) amide;
(iii) amino optionally mono- or di-substituted with C_{1-6} alkyl; amido; or (lower alkyl)amide;
(iv) C_6 or C_{10} aryl or C_{7-16} aralkyl, all optionally substituted with C_{1-6} alkyl, hydroxy, amido, (lower alkyl)amide, or amino optionally mono- or di-substituted with C_{1-6} alkyl; or
(v) Het or (lower alkyl)-Het, both optionally substituted with C_{1-6} alkyl, hydroxy, amido, (lower alkyl) amide, or amino optionally mono- or di-substituted with C_{1-6} alkyl;
$\mathbf{R_5}$ is H or C_{1-6} alkyl; with the proviso that when ~~$\mathbf{R_4}$~~ B is a carboxyl derivative, an amide derivative or a thioamide derivative, $\mathbf{R_4}$ is not ~~(ii)~~ a cycloalkoxy;

Y is H or C_{1-6} alkyl;

$\mathbf{R^3}$ is C_{1-8} alkyl, C_{3-7} cycloalkyl, or C_{4-10} alkylcycloalkyl, all optionally substituted with hydroxy, C_{1-6} alkoxy, C_{1-6} thioalkyl, amido, (lower alkyl)amido, C_6 or C_{10} aryl, or C_{7-16} aralkyl;

B

R^2 is CH_2-R_{20}, NH-R_{20}, O-R_{20} or S-R_{20}, wherein R_{20} is pyrimidinyl, quinazolinyl, (lower alkyl)-pyrimidinyl or (lower alkyl)-quinazolinyl, each optionally mono-, di- or tri-substituted with R_{21},

wherein each R_{21} is independently C_{1-6} alkyl; C_{1-6} alkoxy; lower thioalkyl; sulfonyl; NO_2; OH; SH; halo; haloalkyl; amino optionally mono- or di-substituted with C_{1-6} alkyl, C_6 or C_{10} aryl, C_{7-14} aralkyl, Het or (lower alkyl)-Het; amido optionally mono-substituted with C_{1-6} alkyl, C_6 or C_{10} aryl, C_{7-14} aralkyl, Het or (lower alkyl)-Het; carboxyl; carboxy(lower alkyl); C_6 or C_{10} aryl, C_{7-14} aralkyl or Het, said aryl, aralkyl or Het being optionally substituted with R_{22};

wherein R_{22} is C_{1-6} alkyl; C_{3-7} cycloalkyl; C_{1-6} alkoxy; amino optionally mono- or di-substituted with C_{1-6} alkyl; sulfonyl; (lower alkyl)sulfonyl; NO_2; OH; SH; halo; haloalkyl; carboxyl; amide; (lower alkyl)amide; or Het optionally substituted with C_{1-6} alkyl;

R^1 is H; C_{1-6} alkyl, C_{3-7} cycloalkyl, C_{2-6} alkenyl, or C_{2-6} alkynyl, all optionally substituted with halogen;

or a pharmaceutically acceptable salt or ester thereof;

wherein "Het" is defined as a five-membered saturated or unsaturated, ~~including~~ aromatic or non-aromatic, heterocycle containing from one to four heteroatoms selected from nitrogen, oxygen and sulfur, wherein said heterocycle is optionally fused to a benzene ring.

5. (amended) A compound of formula I according to claim 1, wherein **B** is a carboxyl derivative of formula R_4-O-C(O)-, wherein R_4 is

(i) C_{1-10} alkyl optionally substituted with carboxyl, C_{1-6} alkanoyl, hydroxy, C_{1-6} alkoxy, amino optionally mono- or di-substituted with C_{1-6} alkyl, amido or (lower alkyl)amide;

(ii) C_{3-7} cycloalkyl, C_{4-10} alkylcycloalkyl, all optionally substituted with carboxyl, (C_{1-6} alkoxy)carbonyl, amino optionally mono- or di-substituted with C_{1-6} alkyl, amido or (lower alkyl)amide;

(iv) C_6 or C_{10} aryl or C_{7-16} aralkyl optionally substituted with C_{1-6} alkyl, hydroxy, amido, (lower alkyl)amido, or amino optionally mono- or di-substituted with C_{1-6} alkyl; or

(v) Het or (lower alkyl)-Het, both optionally substituted with C_{1-6} alkyl, hydroxy, amino

B

optionally mono- or di-substituted with C_{1-6} alkyl, amido or (lower alkyl)amido.

6. (amended) A compound of formula I according to claim 1, wherein **B** is an amide derivative of formula $\mathbf{R_4}$-N($\mathbf{R_5}$)-C(O)- wherein $\mathbf{R_4}$ is
(i) C_{1-10} alkyl optionally substituted with carboxyl, C_{1-6} alkanoyl, hydroxy, C_{1-6} alkoxy, amido, (lower alkyl)amido, or amino optionally mono- or di-substituted with C_{1-6} alkyl;
(ii) C_{3-7} cycloalkyl or C_{4-10} alkylcycloalkyl, all optionally substituted with carboxyl, (C_{1-6} alkoxy)carbonyl, amido, (lower alkyl)amido, or amino optionally mono- or di-substituted with C_{1-6} alkyl;
(iii) amino optionally mono- or di-substituted with C_{1-3} alkyl;
(iv) C_6 or C_{10} aryl or C_{7-16} aralkyl, all optionally substituted with C_{1-6} alkyl, hydroxy, amido, (lower alkyl)amide, or amino optionally substituted with C_{1-6} alkyl; or
(v) Het or (lower alkyl)-Het, both optionally substituted with C_{1-6} alkyl, hydroxy, amino optionally substituted with C_{1-6} alkyl, amido or (lower alkyl)amide; and
$\mathbf{R_5}$ is H or methyl.

7. (amended) A compound of formula I according to claim 1, wherein **B** is a thioamide derivative of formula $\mathbf{R_4}$-NH-C(S)-; wherein $\mathbf{R_4}$ is
(i) C_{1-10} alkyl optionally substituted with carboxyl, C_{1-6} alkanoyl or C_{1-6} alkoxy;
(ii) C_{3-7} cycloalkyl or C_{4-10} alkylcycloalkyl, all optionally substituted with carboxyl, (C_{1-6} alkoxy)carbonyl, amino or amido.

11. (amended) A compound of formula I according to claim 5, wherein **B** is a carboxyl derivative of formula $\mathbf{R_4}$-O-C(O)-, wherein $\mathbf{R_4}$ is
(i) C_{1-10} alkyl optionally substituted with carboxyl, C_{1-6} alkanoyl, hydroxy, C_{1-6} alkoxy or amido, (lower alkyl)amide, amino optionally mono- or di-substituted with C_{1-6} alkyl;
(ii) C_{3-7} cycloalkyl, C_{4-10} alkylcycloalkyl, all optionally substituted with carboxyl, (C_{1-6} alkoxy)carbonyl, amido, (lower alkyl)amide, amino optionally mono- or di-substituted with C_{1-6} alkyl, or

B

(iv) C_6 or C_{10} aryl or C_{7-16} aralkyl, all optionally substituted with C_{1-6} alkyl, hydroxy, amino optionally substituted with C_{1-6} alkyl; or
(v) Het or (lower alkyl)-Het, both optionally substituted with C_{1-6} alkyl, hydroxy, amido, or amino optionally mono-substituted with C_{1-6} alkyl.

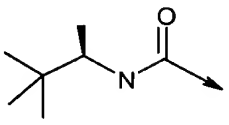
12. (amended) A compound of formula I according to claim 6, wherein **B** is an amide derivative of formula $\mathbf{R_4}$-N($\mathbf{R_5}$)-C(O)- wherein $\mathbf{R_4}$ is
(i) C_{1-10} alkyl optionally substituted with carboxyl, C_{1-6} alkanoyl, hydroxy, C_{1-6} alkoxy, amido, (lower alkyl)amide, amino optionally mono- or di-substituted with C_{1-6} alkyl;
(ii) C_{3-7} cycloalkyl or C_{4-10} alkylcycloalkyl, all optionally substituted with carboxyl, (C_{1-6} alkoxy)carbonyl, amido, (lower alkyl)amide, amino optionally mono- or di-substituted with C_{1-6} alkyl;
(iii) amino optionally mono- or di-substituted with C_{1-3} alkyl, or
(iv) C_6 or C_{10} aryl or C_{7-16} aralkyl, all optionally substituted with C_{1-6} alkyl, hydroxy, amino or amido optionally substituted with C_{1-6} alkyl; or
(v) Het optionally substituted with C_{1-6} alkyl, hydroxy, amino or amido,
and $\mathbf{R_5}$ is H.

13. (amended) A compound of formula I according to claim 7, wherein **B** is a thioamide derivative of formula $\mathbf{R_4}$-NH-C(S)-; wherein $\mathbf{R_4}$ is (i) C_{1-10} alkyl; or (ii) C_{3-7} cycloalkyl.

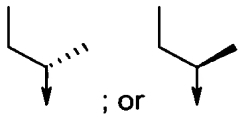
14. (amended) A compound of formula I according to claim 12, wherein **B** is an amide derivative of formula $\mathbf{R_4}$-NH-C(O)- wherein $\mathbf{R_4}$ is
(i) C_{1-10} alkyl optionally substituted with carboxyl, C_{1-6} alkanoyl, hydroxy, C_{1-6} alkoxy amido, (lower alkyl)amide, amino optionally mono- or di-substituted with C_{1-6} alkyl;
(ii) C_{3-7} cycloalkyl or C_{4-10} alkylcycloalkyl, all optionally substituted with carboxyl, (C_{1-6} alkoxy)carbonyl, amido, (lower alkyl)amide, amino optionally mono- or di-substituted with C_{1-6} alkyl;
(iv) C_6 or C_{10} aryl or C_{7-16} aralkyl optionally substituted with C_{1-6} alkyl, hydroxy, amino or

amido.

15. (amended) A compound of formula I according to claim 1, wherein **B** is

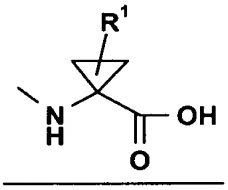
~~*tert*-butoxycarbonyl (Boc)~~ or  .

19. (amended) A compound of formula I according to claim 18, wherein $\mathbf{R^3}$ is the side chain of ~~*tert*-butylglycine (Tbg)~~, Ile, Val, Chg or:


; or .

36. (twice amended) A compound of formula I according to claim 1, wherein ~~**P1 is a cyclobutyl or cyclopropyl ring, both optionally substituted with $\mathbf{R^1}$, wherein $\mathbf{R^1}$**~~ is H, C_{1-3} alkyl, C_{3-5} cycloalkyl, or C_{2-4} alkenyl, all optionally substituted with halo.

37. (amended) A compound of formula I according to claim 36, wherein **P1** is: ~~cyclopropyl~~



and $\mathbf{R^1}$ is ethyl, vinyl, cyclopropyl, 1 or 2-bromoethyl or 1 or 2-bromovinyl.

45. (twice amended) A compound of formula I according to claim 1, wherein **B** is a C_6 or C_{10} aryl or C_{7-16} aralkyl, all optionally substituted with C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkanoyl, hydroxy, hydroxyalkyl, halo, haloalkyl, nitro, cyano, cyanoalkyl, amido, (lower alkyl)amido, or amino optionally substituted with C_{1-6} alkyl; or

B

Het or (lower alkyl)-Het, all optionally substituted with C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} alkanoyl, hydroxy, hydroxyalkyl, halo, haloalkyl, nitro, cyano, cyanoalkyl, amido, (lower alkyl)amido, or amino optionally substituted with C_{1-6} alkyl,. or

B is $\mathbf{R_4}$-SO_2 wherein $\mathbf{R_4}$ is ~~preferably~~ amido; (lower alkyl)amide; C_6 or C_{10} aryl, C_{7-14} aralkyl or Het, all optionally substituted with C_{1-6} alkyl, or

B is an acyl derivative of formula $\mathbf{R_4}$-C(O)- wherein $\mathbf{R_4}$ is

(i) C_{1-10} alkyl optionally substituted with carboxyl, hydroxy or C_{1-6} alkoxy, amido, (lower alkyl)amide, or amino optionally mono- or di-substituted with C_{1-6} alkyl;

(ii) C_{3-7} cycloalkyl or C_{4-10} alkylcycloalkyl, both optionally substituted with hydroxy, carboxyl, (C_{1-6} alkoxy)carbonyl, amido, (lower alkyl)amide, or amino optionally mono- or di-substituted with C_{1-6} alkyl;

(iv) C_6 or C_{10} aryl or C_{7-16} aralkyl, all optionally substituted with C_{1-6} alkyl, hydroxy, amido, (lower alkyl)amide, or amino optionally substituted with C_{1-6} alkyl;

(v) Het or (lower alkyl)-Het, both optionally substituted with C_{1-6} alkyl, hydroxy, amino optionally substituted with C_{1-6} alkyl, amido, (lower alkyl)amide, or amino optionally substituted with C_{1-6} alkyl, or

B is a carboxyl derivative of formula $\mathbf{R_4}$-O-C(O)-, wherein $\mathbf{R_4}$ is

(i) C_{1-10} alkyl optionally substituted with carboxyl, C_{1-6} alkanoyl, hydroxy, C_{1-6} alkoxy, amino optionally mono- or di-substituted with C_{1-6} alkyl, amido or (lower alkyl)amide;

(ii) C_{3-7} cycloalkyl, C_{4-10} alkylcycloalkyl, all optionally substituted with carboxyl, (C_{1-6} alkoxy)carbonyl, amino optionally mono- or di-substituted with C_{1-6} alkyl, amido or (lower alkyl)amide;

(iv) C_6 or C_{10} aryl or C_{7-16} aralkyl optionally substituted with C_{1-6} alkyl, hydroxy, amido, (lower alkyl)amido, or amino optionally mono- or di-substituted with C_{1-6} alkyl; or

(v) Het or (lower alkyl)-Het, both optionally substituted with C_{1-6} alkyl, hydroxy, amino optionally mono- or di-substituted with C_{1-6} alkyl, amido or (lower alkyl)amido, or

B is an amide derivative of formula $\mathbf{R_4}$-N($\mathbf{R_5}$)-C(O)- wherein $\mathbf{R_4}$ is

(i) C_{1-10} alkyl optionally substituted with carboxyl, C_{1-6} alkanoyl, hydroxy, C_{1-6} alkoxy, amido, (lower alkyl)amido, or amino optionally mono- or di-substituted with C_{1-6} alkyl;

B

(ii) C_{3-7} cycloalkyl or C_{4-10} alkylcycloalkyl, all optionally substituted with carboxyl, (C_{1-6} alkoxy)carbonyl, amido, (lower alkyl)amido, or amino optionally mono- or di-substituted with C_{1-6} alkyl;

(iii) amino optionally mono- or di-substituted with C_{1-3} alkyl;

(iv) C_6 or C_{10} aryl or C_{7-16} aralkyl, all optionally substituted with C_{1-6} alkyl, hydroxy, amido, (lower alkyl)amide, or amino optionally substituted with C_{1-6} alkyl; or

(v) Het or (lower alkyl)-Het, both optionally substituted with C_{1-6} alkyl, hydroxy, amino optionally substituted with C_{1-6} alkyl, amido or (lower alkyl)amide; and

R_5 is H or methyl, or

B is thioamide derivative of formula **R_4**-NH-C(S)-; wherein **R_4** is

(i) C_{1-10} alkyl optionally substituted with carboxyl, C_{1-6} alkanoyl or C_{1-6} alkoxy;

(ii) C_{3-7} cycloalkyl or C_{4-10} alkylcycloalkyl, all optionally substituted with carboxyl, (C_{1-6} alkoxy)carbonyl, amino or amido;

Y is H or methyl;

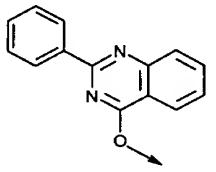
R^3 is C_{1-8} alkyl, C_{3-7} cycloalkyl, or C_{4-10} alkylcycloalkyl, all optionally substituted with hydroxy, C_{1-6} alkoxy, C_{1-6} thioalkyl, acetamido, C_6 or C_{10} aryl, or C_{7-16} aralkyl;

R^2 is S-**R_{20}** or O-**R_{20}** wherein **R_{20}** is pyrimidinyl, quinazolinyl, -CH_2-pyrimidinyl or -CH_2-quinazolinyl, all optionally mono-, di- or tri-substituted with **R_{21}**, wherein

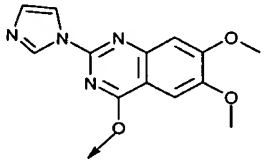
R_{21} is C_{1-6} alkyl; C_{1-6} alkoxy; lower thioalkyl; amino or amido optionally mono-or di-substituted with C_{1-6} alkyl, C_6 or C_{10} aryl, C_{7-16} aralkyl, Het or (lower alkyl)-Het; NO_2; OH; halo; trifluoromethyl; carboxyl; C_6 or C_{10} aryl, C_{7-16} aralkyl, or Het, said aryl, aralkyl or Het being optionally substituted with **R_{22}**, wherein

R_{22} is C_{1-6} alkyl; C_{3-7} cycloalkyl; C_{1-6} alkoxy; amino; mono- or di-(lower alkyl)amino; (lower alkyl)amide; sulfonylalkyl; NO_2; OH; halo; trifluoromethyl; carboxyl or Het; or

R^2 is selected from the group consisting of:



; and

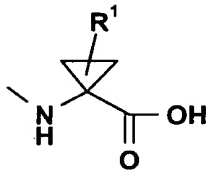


;

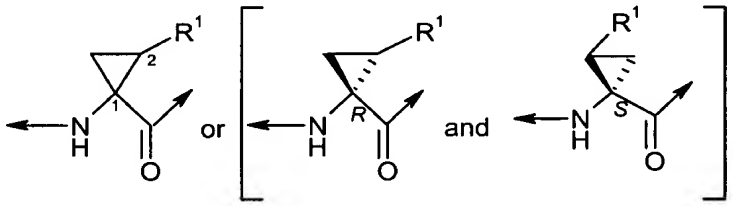
B

and

~~the~~ **P1** ~~segment~~ is:



~~a cyclopropyl ring, both optionally substituted with R^1~~, wherein R^1 is H, C_{1-3} alkyl, C_{3-5} cycloalkyl, or C_{2-4} alkenyl optionally substituted with halo, and said R^1 at carbon 2 is orientated *syn* to the carbonyl at position 1, represented by the radical:



;

or a pharmaceutically acceptable salt or ester thereof.

REMARKS

The specification and claims have been amended for clarification and to specifically address the issues raised by the Examiner. Support for these amendments is present in the application as filed. Support for certain specific amendments is also discussed in detail below. There being no issue of new matter, entry of the foregoing amendments is respectfully requested.